NDA 19-979/S-017

JUL 28 1999

Syntex (U.S.A) Inc.
c/o Hoffinann-La Roche Inc.
Attention: Ms. Margaret Jack
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Ms. Jack:

Please refer to your supplemental new drug application dated February 1, 1999, received February 2, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ticlid (ticlopidine hydrochloride) Tablet, 250 mg.

We acknowledge receipt of your submission dated July 7, 1999.

This supplemental new drug application provides for final printed labeling revised by changing the **BOXED WARNING** of the package insert and the replacement of the manufacturer information with distributor information.

These changes are as follows:

1. The information regarding thrombotic thrombocytopenic purpura (TTP) in the **BOXED WARNING** of the package insert has been revised to reflect the finding of one case of TTP that occurred during the conduct of the clinical studies as follows:

   The first sentence in the third paragraph of the **BOXED WARNING** has been changed from the following sentence:

   > Thrombotic thrombocytopenic purpura was not seen during clinical trials, but US physicians reported about 100 cases between 1992 and 1997.

   to the following two sentences:

   > One case of thrombotic thrombocytopenic purpura was reported during clinical trials. Based on postmarketing data, US physicians reported about 100 cases between 1992 and 1997.

2. In addition, the "Manufactured by" information has been replaced with that regarding the distributor as follows:

   The "Manufactured by" information has been changed from the following:

Manufactured by Syntex Puerto Rico, Inc.
Humacao, Puerto Rico 00791
or Oread Inc.
Palo Alto, California 94304

for:

(Roche Hexagon) Pharmaceuticals

Roche Laboratories Inc.
340 Kingsland Street
Nutley, New Jersey 07110-1199

27091807-0698 Revised: June 1998

to the following:

Distributed by:
(Roche Hexagon)
Pharmaceuticals
Roche Laboratories Inc.
340 Kingsland Street
Nutley, New Jersey 07110-1199

XXXXXXXXXXXXX

Revised: XXXX 1999

In our June 8, 1999 approvable letter, it was noted that the copyright statement had been relocated to the section at the end of the package insert containing the distributor information. In a July 15, 1999 telephone conversation between Ms. Elisa Mandra, a representative of Hoffrnann-LaRoche and Ms. Colleen LoCicero, Regulatory Health Project Coordinator, Division of Cardio-Renal Drug Products, Ms. Mandra explained that the copyright statement had not been relocated and that you have an agreement with your printer that the copyright statement that appears at the end of the draft package insert is to be printed at the bottom of the first column of text in the final printed package insert.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling included in your June 7, 1999 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MED WATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Ms. Colleen LoCicero
Regulatory Health Project Coordinator
(301) 594-5312

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research